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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
GOLLAMUDI, SHARMILA S	

ART UNIT	PAPER NUMBER
1616	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/886,296	TARARA ET AL.	
	Examiner	Art Unit	
	Sharmila S. Gollamudi	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 January 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4-15,18-23,39-47 and 49-56* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4-15, 18-23, 39-47, and 49-56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Receipt of Request for Continued Examination filed in January 13, 2005 is acknowledged. Claims **4-15, 18-23, 39-47, and 49-56** are pending in this application. Claims 1-3, 16-17, 24-38, and 48 stand cancelled.

Response to Arguments

Applicant's arguments with respect to claims 4-15, 18-23, 39-47, and 49-56 have been considered but are moot in view of the new ground(s) of rejection. However, since the examiner has retained Hanes as the primary reference, the examiner will address the remarks pertaining to Hanes.

Applicant argues that Hanes et al do not teach bulk density and rather teaches tap density. Applicant argues that the limitation that the phospholipid comprises a gel to crystal transition temperature of greater than 40 degrees Celsius is not disclosed.

Applicant's arguments have been fully considered but they are not persuasive. Firstly, the examiner points that Hanes teaches tap density is a standard measure of the envelope mass density (bulk density) on column 9, lines 5-6. On column 14, lines 36-40, Hanes teaches the bulk density is estimated by tap density measurements. Thus, Hanes discloses that tap density measurements are in essence a bulk density measurement and Hanes clearly teaches a density of less than 0.1. Therefore, this argument is moot.

With regard to the limitation of claim 40, the examiner points out that Hanes teaches the same phospholipids and this limitation is an inherent feature of the claimed phospholipids. Thus, the prior art need not recognize every inherent property of an element to read on the claim.

Further, the examiner provides US 5,776,488 as art of interest wherein Mori et al discloses DPPC has a transition temperature of 42 degrees Celsius. See column 3, lines 40-45.

Applicant argues that Hanes does not teach the mean aerodynamic diameter and for instance, a particle density of 0.1 g/cm3 will be roughly three time smaller than the geometric diameter. The examiner points out that this is exactly what Hanes teaches on column 9. Hanes teaches that if the particle, for instance, has a geometric diameter of 9.5 microns, according to the equation on column 9, the aerodynamic diameter would be 3 microns. Further, Hanes teaches a geometric diameter of 5-30 microns and states on column 9, lines 25-27 the particles have a small aerodynamic diameter in comparison to the actual envelope sphere diameter (geometric diameter). Therefore, if the geometric diameter is 5 microns, then the aerodynamic diameter is less than 5 microns since Hanes teaches the aerodynamic diameter is less than the geometric diameter. Therefore, this argument is moot.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 8-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 8 and 9 respectively are directed to the powder composition of independent claim 39 "wherein the powder composition has a fine particle fraction of greater than" which is vague and indefinite since it is unclear what the fine particle fraction is referring to. Is this fine particle fraction referring to the microstructure particles claimed in the independent claim and the weight

percent of the microstructures in the entire powder composition or is this fine particle fraction referring to a carrier powder in combination with the microstructure particles? Further clarification is requested since the intended limitation is unclear.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 40, 47, and 56 are rejected under 35 U.S.C. 102(e) as being anticipated by Unger (6,120,751).

Unger discloses charged lipids and their use for drug delivery, targeted delivery, etc. See abstract. The composition comprises a charged lipid, a counter ion, a lipid covalently bonded to a polymer, and a bioactive agent. See column 2, lines 20-30. The composition is in the form of a vesicle including liposomes and micelles. See column 4, lines 19-45. The vesicles preferably have diameters of less than about 30 microns and more preferably less than about 12 microns. See column 68, lines 1-6. Note vesicles are spherical bodies and have a micron size range and thus read on "microstructure". Specifically, example 2 discloses the composition comprising instantly claimed dipalmitoylphosphatidylcholine (DPPC), dipalmitoylphosphatidic acid (DPPA), dipalmitoylphosphatidylethanolamine-polyethylene glycol-5,000 (DPPE-PEG5,000), and calcium chloride. Example 13 discloses lyophilizing the composition of example 2 to yield a dry powder. Unger discloses the lipid composition is useful for delivering bioactive agents to a

patient's lungs. For pulmonary applications, dried or lyophilized powdered compositions are administered via an inhaler.

With regard the recitation of "wherein said phospholipids comprises a gel to liquid crystal transition temperature of greater than 40 degrees Celsius, page 14, of the instant specification discloses that dipalmitoylphosphatidylcholine falls within this category. Secondly, the examiner cites US 5,776,488 as art of interest wherein Mori et al discloses DPPC has a transition temperature of 42 degrees Celsius. See column 3, lines 40-45. Further, DPPC is zwitterionic phospholipid.

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 40, 47, and 56 are rejected under 35 U.S.C. 102(a) as being anticipated by Eistetter (WO 97/26863).

Eistetter discloses a powder comprising 7g of dipalmitoylphosphatidylcholine, 205mg calcium chloride, and 250mg palmitic acid. See example 1. The particle size is between 1-5 microns. See claim 11. Note that it is the examiner's position that palmitic acid reads on the broad recitation "active agent" since fatty acids are know to be used as active agents.

With regard to "microstructure", Eistetter teaches spray drying a solution of 7g of dipalmitoylphosphatidylcholine, 205mg calcium chloride, and 250mg palmitic acid to yield individual particles which reads on "microstructure".

With regard the recitation of "wherein said phospholipids comprises a gel to liquid crystal transition temperature of greater than 40 degrees Celsius, page 14, of the instant specification discloses that dipalmitoylphosphatidylcholine falls within this category. Secondly, the examiner cites US 5,776,488 as art of interest wherein Mori et al discloses DPPC has a

transition temperature of 42 degrees Celsius. See column 3, lines 40-45. Further, DPPC is zwitterionic phospholipid.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 4-15, 18-23, 39-47, 49-50, and 55-56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hanes et al (US 5,855,913) in view of Unger (6,120,751).

Hanes et al teach aerodynamically light particles for drug delivery to the pulmonary system. The particles have a tap density of less than 0.4 g/cm3, aerodynamic diameter of 3 microns (see column 9, line 45-50), and a mass mean diameter (geometric diameter) between 5 to 30 microns. See abstract, See column 9, lines 26-45, and claim 1. Claim 3 teaches a tap density of less than 0.1 g/cm3. Table 2 teaches the porous microparticles with DPPC have a density of 0.30 g/cm3. It should be noted that Hanes teaches tap density is a standard measure of

the envelope mass density (bulk density) on column 9, lines 5-6. On column 14, lines 36-40, Hanes teaches the bulk density is estimated by tap density measurements.

Hanes the presence of irregular surface structure, or pores or cavities within the particle (this reads on instantly claimed "hollow microstructure") contributes to the aerodynamic lightness. Hanes also teaches the irregular surface texture and porous structure also contributes to the low tap density and manipulation of these features permits the delivery of larger particle envelope volumes into the lungs (col. 9, lines 10-25). Porosity and surface roughness can be increased by varying the inlet and outlet temperatures, among other factors. See column 12, lines 10-13. The aerodynamically light particles may be fabricated to provide a particle sample with a preselected size distribution. For example, greater than 30%, 50%, 70%, or 80% of the particles in a sample can have a geometric diameter within a selected range of at least 5 microns. The particles contain surfactants such as DPPC (instant gel to liquid temperature; see US 5,776,488 as art of interest) and the microstructures are taught to encapsulate active agents, which allows the active to remain protected (col. 10, lines 37-50 and examples). Note that DPPC is a zwitterionic lipid. The particles can also be co-delivered with larger carrier particles, not carrying a therapeutic agent, having, for example, a mean diameter ranging between about 50 microns and 100 microns. See column 4, lines 12-15.

Biodegradable polymer, copolymers, or a blend may be utilized. Hanes teaches the use of polyglycolic acid and polylactic acid with a surfactant (DPPC) may be utilized and the polyester may also have a charged or functionizable groups such as amino acids. Other polymers taught are acrylic acids and methacrylic acids and polyvinyl compounds may be used to make the microsphere. See column 5, line 49 to column 6, line 27. Further, the particles may be formed

into microspheres by methods such as coacervation, interfacial polymerization, etc. (note col. 6). Instant therapeutic agents including insulin, growth hormones, etc. are taught on column 10, lines 4-30.

Hanes teaches aerodynamically light PEG particles were prepared by spray drying using 5 g PEG (MW 15,000-20,000, Sigma) and the surfactant such as DPPC may be incorporated into the polymer solution prior to particle formation, or optionally the particles can be ionically or covalently coated by surfactant on the particle surface after particle formation, or the surfactant may be absorbed onto the particle surface. See column 13, lines 1-25.

Hanes et al do not teach the use of calcium in the structural matrix.

Unger teaches charged lipids and their use for drug delivery, targeted delivery, etc. See abstract. Unger teaches prior art studies have described the effects of calcium and other multivalent cations on membrane asymmetry, lipid distribution, vesicle size, aggregation and fusion. The general consensus exists that multivalent cations, such as calcium and magnesium, in the external environment of phospholipid vesicles cause the structures to aggregate into larger, multilamellar structures and promotes fusion. Unger's composition comprises a charged lipid, a counter ion, a lipid covalently bonded to a polymer, and a bioactive agent. See column 2, lines 20-30. The composition is in the form of a vesicle including liposomes and micelles, which can be solid or porous. See column 4, lines 19-45. The vesicles preferably have diameters of less than about 30 microns and more preferably less than about 12 microns. See column 68, lines 1-6. The charged lipid may be anionic (i.e., negatively charged, that is, carrying a net negative charge) or cationic (i.e., positively charged, that is, carrying a net positive charge). See column 11, lines 5-10. A cationic counter ion is used to form the compositions. Preferred cations are

calcium, magnesium, and zinc, and paramagnetic cations such as manganese and gadolinium. Most preferably the cation is calcium. See column 12, lines 1-5. Specifically, example 2 teaches the composition comprising instantly claimed dipalmitoylphosphatidylcholine (DPPC), dipalmitoylphosphatidic acid (DPPA), dipalmitoylphosphatidylethanolamine-polyethylene glycol-5,000 (DPPE-PEG5,000), and calcium chloride. Example 13 discloses lyophilizing the composition of example 2 to yield a dry powder. Unger teaches the lipid covalently bonded to a polymer (e.g., DPPE-PEG-5,000) causes compaction of the size of the composition in the presence of a counter ion, such as calcium, when compared to the corresponding compositions that do not contain a counter ion. The compaction effect caused by the lipid covalently bonded to the polymer is most notable when the counter ion is added at the initial incubation of the lipid mixture. Increasing the amount of the lipid covalently bonded to a polymer allows the composition to stabilize in the presence of a counter ion. When the lipid covalently bonded to the polymer is present in an amount less than about 5%, the composition is generally unstable and may precipitate. See column 10, lines 50-55. Unger discloses the lipid composition is useful for delivering bioactive agents to a patient's lungs. For pulmonary applications, dried or lyophilized powdered compositions are administered via an inhaler.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Hanes and Unger and utilize calcium in the microstructures of Hanes. One would have been motivated to utilize calcium in the formation of Hanes's particles since Unger teaches the use of a cations such as calcium promotes fusion of the phospholipids and stabilizes compaction of phospholipid-polymer containing particles, specifically in a PEG-phospholipid particle. Further, a skilled artisan would have expected the

same stabilizing effect in Hanes's particles since Hanes also teaches a particle comprising PEG and a phospholipid.

With regard to the claims 4-5 (porosity), claims 6-7 (pore size), and claim 13 (shell thickness), although Hanes does not specify the porosity in terms of weight percent as instantly claimed, specify the pore size, or the shell thickness, it is the examiner's position that the Hanes would have a similar porosity, pore size, and shell thickness as instantly claimed for the following reason: Hanes teaches a substantially similar particle with instant bulk density (measured by tap density), instant geometric diameter, and instant aerodynamic diameter. Thus, "when a structure recited in the reference is substantially identical to that of the claims, claimed properties are presumed to be the inherent". See MPEP 2112.01. Further, Hanes teaches the porous and light nature of the microstructure contributes to the properties such as the low tap density of the particle and Hanes teaches the same density as claimed; thus the pore size and porosity must be similar as instantly claimed. Further, since the shell thickness also would contribute to the density of the particles and the prior art teaches the same density as claimed, it is the examiner's position that the prior art would have the same shell thickness as claimed. It should be noted that the examiner has provided a rationale as to why Hanes's particle would have the same or similar porosity, pore size, and shell thickness; thus the burden has shifted to the applicant to provide evidence to the contrary. See MPEP 2112.

Furthermore, assuming arguendo that Hanes's porosity, pore size, and shell thickness are not the same as instantly claimed, the manipulation of these parameters is considered prima facie obvious to one of ordinary skill in the art since Hanes provides the guidance in which the various factors can be manipulated (column 9 and examples) to yield the desired property. For instance,

Hanes teaches manipulating the outlet and inlet temperature when making the particles to manipulate the porosity. Further, Hanes teaches the manipulation of surface roughness (porosity), diameter, and tap density, determine the delivery site of the particles in the lungs (lower lung region or upper lung region). (col. 8, lines 19-68 and column 9). Therefore, a skilled artisan would have been motivated to look at the guidance of Hanes and manipulate the above factors and fabricate the microstructure according to the lung region to be targeted.

Claim 51-52 under 35 U.S.C. 103(a) as being unpatentable over Hanes et al (US 5855913) in view of Unger (6,120,751) in further view of Igarashi et al (4201774).

The detailed teaching of Hanes and Unger have been set forth above. Hanes et al teach dry powder inhaler compositions. Hanes teaches several active agents including antibiotics in the composition. Unger teaches the use of calcium to stabilize the phospholipids.

Hanes does not teach the specific use of aminoglycoside antibiotic.

Igarashi et al teaches aminoglycoside antibiotics for the treatment of gram-positive and gram-negative bacteria.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the instant medicament in Hanes et al's composition. One would be motivated to do so since the instant antibiotics treats gram-positive and gram-negative bacteria and depending on the patient's requirement, the appropriate drug is used. One would have expected similar results since Hanes teaches the suitability of antibiotics as the active agent. Therefore, the selection of a particular drug for use in the composition is considered prima facie obvious since the selection depends on the symptoms and disease being treated.

Claims 53-54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hanes et al (US 5855913) in view of Unger (6,120,751) in further view of Benson et al (5,006,343).

The detailed teaching of Hanes and Unger have been set forth above. Hanes et al teach dry powder inhaler compositions. Hanes teaches several active agents including antibiotics in the composition. Unger teaches the use of calcium to stabilize the phospholipids.

Hanes does not teach the specific use of fungicides.

Benson et al teach pulmonary administration of active agents to treat pulmonary diseases. Suitable drugs that may be administered for lung specific disease include fungicides. See column 10, lines 33-45.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use a fungicide in Hanes et al's composition. One would be motivated to do so since Benson et al teach the use of array of medications including fungicides that are useful for treating lung diseases. Therefore, the selection of a particular drug for use in the composition is considered prima facie obvious since the selection depends on the symptoms and disease being treated.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 4-15, 18-23, 39-47, and 49-56 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 6-7, 9-10, 46-50, 54-57, 59, 61-67, 69-70, 74-77, 79-90 of copending Application No. 09/568818. Although the conflicting claims are not identical, they are not patentably distinct from each other because:

The instant application claim 39 is directed to a powder composition comprising microstructures comprising an active agent, calcium, and a phospholipid in the matrix, with a geometric diameter of 1-30 microns, a bulk density of less than about 0.5 g/cm3, and an aerodynamic diameter of less than 5 microns. Independent claim 40 is directed to a powder composition comprising microstructures comprising an active agent, calcium, and a phospholipid in the matrix wherein said phospholipids comprises a gel to liquid crystal transition temperature of greater than 40 degrees Celsius. Dependent claims are directed to active agents selected from antiinflammatories, lung surfactants, antibiotics, antifungals, insulin, etc. The phospholipid is selected from dilauroylphosphatidylcholine, dioleylphosphatidylcholine, dipalmitoylphosphatidylcholine, disteroylphosphatidylcholine, dibehenoylphosphatidylcholine, and diarachidoylphosphatidylcholine, and combinations.

Copending independent claims 46, 59, and 82 are directed to a microparticle comprising an active agent and a metal-ion complex with a density as measured by He displacement is 0.5-2 g/ml. Calcium is one of the metal ion species claimed in a dependent claim. Dependent claims are directed to phospholipids and specifically selected from the group comprising

"dipalmitoylphosphatidylcholine, disteroylphosphatidylcholine, and dimyristylphosphatidylcholine". Dependent claims are directed to the same active agents as claimed in instant application. Dependent claims are directed to an aerodynamic particle size of 0.5-7 microns. Dependent claims are directed to dry powder. Dependent claim are directed to a zwitterionic lipid.

The instant application and '818 are different in that firstly '818 independent claims do not recite a phospholipid; however the dependent claims further comprise phospholipids, more specifically, the instant phospholipids. Thus, the instant application and copending application have overlapping subject matter wherein both application are directed to microparticles comprising the critical elements of 1) an active agent, 2) a phospholipid, and 3) a metal ion. Secondly, '818 is directed to the broad scope of the metal ion and the instant application is directed to the metal ion species calcium; however, '818 claims calcium in the dependent claims. Further, '818 is broadly directed to microparticles without claiming the density, the geometric diameter, pore size, etc.; however '818 encompasses the scope of the instant microstructures and the respective properties, which is the narrower scope. Lastly, it should be noted with regard to instant claim 40, although '818 does not specifically claim "phospholipids comprises a gel to liquid crystal transition temperature of greater than 40 degrees Celsius", '818 does claim DPPC in the dependent claims and DPPC has a temperature of 42 degrees Celsius.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 4-15, 18-23, 39-47, and 49-56 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-

3, 8-9, 11-15, 17, 19-25, 29-32, 53-55, 57-62, 64-66, 67-89 of copending Application No. 09/851226. Although the conflicting claims are not identical, they are not patentably distinct from each other because:

The instant application claim 39 is directed to a powder composition comprising microstructures comprising an active agent, calcium, and a phospholipid in the matrix, with a geometric diameter of 1-30 microns, a bulk density of less than about 0.5 g/cm3, and an aerodynamic diameter of less than 5 microns. Independent claim 40 is directed to a powder composition comprising microstructures comprising an active agent, calcium, and a phospholipid in the matrix wherein said phospholipids comprises a gel to liquid crystal transition temperature of greater than 40 degrees Celsius. Dependent claims are directed to active agents selected from antiinflammatories, lung surfactants, antibiotics, antineoplastics, antifungals, specifically insulin, growth factors etc. The phospholipid is selected from dilauroylphosphatidylcholine, dioleylphosphatidylcholine, dipalmitoylphosphatidylcholine, disteroylphosphatidylcholine, dibehenoylphosphatidylcholine, and diarachidoylphosphatidylcholine, and combinations.

'226 is directed to a particulate composition comprising an active agent, a saturated phospholipid, and a polyvalent cation, wherein the ratio of the polyvalent cation to phospholipid is at least 0.05 and is sufficient high to increase the gel-to-liquid crystal transition temperature of the particles without the cation. Dependent claims are directed to calcium as the metal ion. Dependent claim is directed to a gel to liquid crystal transition temperature of greater than 40 degrees Celsius. Dependent claims are directed to the same active agent insulin and growth hormones. Dependent claims are directed to a mass median diameter of 0.5-5 microns, an aerodynamic diameter of 0.5-5 microns, and a bulk density of less than 0.5 and 0.05 respectively.

The phospholipid is selected from dipalmitoylphosphatidylcholine and disteroylphosphatidylcholine.

The instant application and '226 are different in that '226 is directed to the broad scope of the metal ion and the instant application is directed to the metal ion species calcium; however, '226 claims calcium in the dependent claims. Further, '226 claims the amount of the cation to increase the gel to liquid transition temperature and the instant application does not recite any concentration of the cation. However, the manipulation of concentrations are considered to be prima facie obvious. See In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). Thus, the instant application and copending application have overlapping subject matter wherein both application are directed to microparticles comprising the critical elements of 1) an active agent, 2) a phospholipid, and 3) a metal ion.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 4-15, 18-23, 39-47, and 49-56 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-15, 19-22, 37-49, 52-64, 67-79, 82-83, 94, and 102 of copending Application No. 10/750934. Although the conflicting claims are not identical, they are not patentably distinct from each other because:

The instant application claim 39 is directed to a powder composition comprising microstructures comprising an active agent, calcium, and a phospholipid in the matrix, with a geometric diameter of 1-30 microns, a bulk density of less than about 0.5 g/cm3, and an aerodynamic diameter of less than 5 microns. Independent claim 40 is directed to a powder

composition comprising microstructures comprising an active agent, calcium, and a phospholipid in the matrix wherein said phospholipids comprises a gel to liquid crystal transition temperature of greater than 40 degrees Celsius. Dependent claims are directed to active agents selected from antiinflammatories, lung surfactants, antibiotics, antineoplastics, antifungals, specifically insulin, growth factors etc. The phospholipid is selected from dilauroylphosphatidylcholine, dioleylphosphatidylcholine, dipalmitoylphosphatidylcholine, disteroylphosphatidylcholine, dibehenoylphosphatidylcholine, and diarachidoylphosphatidylcholine, and combinations.

'934 is directed to a pharmaceutical composition comprising particles comprising an active ingredient in a lipid matrix. The particles have a geometric diameter of less than 3 microns and a mass median diameter of less than 20 microns. Dependent claims are directed to a lipid selected from dipalmitoylphosphatidylcholine, disteroylphosphatidylcholine, dibehenoylphosphatidylcholine, and diarachidoylphosphatidylcholine. Dependent claims are directed to hollow, porous particles with a bulk density of less than 0.5 g/cm3, 0.3 g/cm3, and 0.2 g/cm3. Dependent claims are directed to the particle further comprising a polyvalent cation and the specification defines the polyvalent cation as calcium, magnesium, and iron. Independent claim is directed to a specific active agent, amphotericin.

Copending application and instant application are different because '934's independent claim is not directed to a metal ion. However, the independent claims have comprising language and the dependent claim is directed to the particle further comprising polyvalent metal ions. Thus, the combination of a polyvalent ion, phospholipid, and active agent renders a scope that encompasses the scope of the instant application. Thus, both application are directed to

microparticles comprising the critical elements of 1) an active agent, 2) a phospholipid, and 3) a metal ion.

Claims 4-15, 18-23, 39-47, and 49-56 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-27, 32-39 of copending Application No. 10/982191. Although the conflicting claims are not identical, they are not patentably distinct from each other because:

The instant application claim 39 is directed to a powder composition comprising microstructures comprising an active agent, calcium, and a phospholipid in the matrix, with a geometric diameter of 1-30 microns, a bulk density of less than about 0.5 g/cm3, and an aerodynamic diameter of less than 5 microns. Independent claim 40 is directed to a powder composition comprising microstructures comprising an active agent, calcium, and a phospholipid in the matrix wherein said phospholipids comprises a gel to liquid crystal transition temperature of greater than 40 degrees Celsius. Dependent claims are directed to active agents selected from antiinflammatories, lung surfactants, antibiotics, antineoplastics, antifungals, specifically insulin, growth factors etc. The phospholipid is selected from dilauroylphosphatidylcholine, dioleylphosphatidylcholine, dipalmitoylphosphatidylcholine, disteroylphosphatidylcholine, dibehenoylphosphatidylcholine, and diarachidoylphosphatidylcholine, and combinations.

'191 is directed to a pharmaceutical composition comprising active ingredient and a lipid wherein the gel to liquid crystal transition temperature of greater than 57 degrees Celsius. The dependent claims are directed to the lipid components selected from dipalmitoylphosphatidylcholine. Dependent claims further comprises a divalent cation, specifically calcium. Dependent claims are directed to composition in a dry powder form

wherein the particles are hollow and porous particles. Dependent claims are directed to the particles having a geometric diameter of less than 20 microns. Dependent claims are directed to the particles with a bulk density of less than 0.5 g/cm3, 0.3 g/cm3, and 0.2 g/cm3.

Copending application and instant application are different since '934's independent claim is not directed to a metal ion. However, the independent claims have comprising language and the dependent claim is directed to the particle further comprising polyvalent metal ions, specifically calcium ions. Thus, the combination of a polyvalent ion, phospholipid, and active agent renders a scope that encompasses the scope of the instant application. Thus, both application are directed to microparticles comprising the critical elements of 1) an active agent, 2) a phospholipid, and 3) a metal ion.

Pertinent Prior Art

PGPUB 20020052310 with an effective filing date of 12/29/00 and claiming benefit to US provisional 60/05004 filed 9/15/97 is considered pertinent to applicant's disclosure but does not constitute prior art since the pertinent subject matter regarding divalent cations in section [0093] is not supported in the provisional application of 60/05004. The subject matter claimed in the instant application is supported in US provisional application 60/060337 which has a filing date of 9/29/97.

Conclusion

All the claims are rejected at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharmila S. Gollamudi whose telephone number is 571-272-0614. The examiner can normally be reached on M-F (8:00-5:30), alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on 571-272-0887. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Sharmila S. Gollamudi
Examiner
Art Unit 1616

SSG